I. AMENDMENTS

IN THE CLAIMS

Cancel claims 9-13 and 16-19 without prejudice to renewal.

Please enter new claim 23, as shown below.

1. (Previously presented) A gene-targeted mouse comprising a modified endogenous apolipoprotein E (apoE) allele, wherein said modified allele comprises an apoE-encoding nucleic acid under transcriptional control of endogenous regulatory sequences, wherein the modified allele encodes a modified apoE polypeptide that exhibits domain interaction characteristic of human apolipoprotein E4 (apoE4), wherein the modified apoE polypeptide comprises a Thr → Arg substitution at a position equivalent to amino acid 61 of human apoE4, and wherein the modified apoE polypeptide exhibits preferential binding to lower density lipoproteins.

2. (Canceled)

3. (Previously presented) The gene-targeted mouse of claim 1, wherein the gene-targeted mouse is homozygous for the modified apoE allele.

4. (Canceled)

5. (Previously presented) A cell isolated from the gene-targeted mouse of claim 1, wherein said cell produces the modified apoE polypeptide.

6. (Canceled)

7. (Previously presented) The cell of claim 5, wherein the cell is homozygous for the modified apoE allele.

8.-13. (Canceled)

14. (Previously presented) A method of identifying an agent that reduces a phenomenon associated with Alzheimer's disease (AD), the method comprising:

a) contacting the gene-targeted mouse of claim 1 with a test agent; and

b) determining the effect of the test agent on reducing a phenomenon associated with AD.

15. (Previously presented) The method of claim 14, wherein the phenomenon associated with AD is selected from the group consisting of amyloid deposits, neuronal cell loss, and neurofibrillary tangles.

16.-19. (Canceled)

20. (Previously presented) The cell according to claim 5, wherein said cell is an astrocyte.

21. (Previously presented) The cell according to claim 5, wherein said cell is a microglial cell.

22. (Previously presented) The cell according to claim 5, wherein the cell is a neuronal cell.

23. (New) The gene-targeted mouse of claim 1, wherein the mouse exhibits apoE4-related neurodegeneration.